

In re Application of:

Zuker et al.

Application No.: 09/462,517

Filed: May 18, 2000

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Atty. Docket No.: VERT1210-1 (formerly AURO1120-1)

**Amendments to the Claims:**

Please cancel claims 1-13 and 16 to 35, without prejudice or disclaimer.

Please amend claim 43 as indicated in the Listing of Claims.

**Listing of Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-13 (Canceled)

14. (Previously presented): A method of identifying a modulator of signal transduction affected by an Inactivation No Afterpotential D (InaD) protein, comprising:

- a) contacting a first cell with a test chemical,  
wherein said first cell comprises at least one signal transduction protein and a polynucleotide encoding a transducisome protein, and said transducisome protein functionally binds to said signal transduction protein to permit or enhance signal transduction, and wherein the transducisome protein is InaD,
- b) activating said signal transduction in said first cell,
- c) detecting said signal transduction from said first cell with a signal transduction detection system,
- d) contacting a second cell with said test chemical,  
wherein said second cell comprises said signal transduction protein and a polynucleotide encoding a defective InaD protein that fails to functionally bind at least one signal transduction protein to permit or enhance signal transduction, and wherein the defective InaD protein comprises an amino acid mutation in a PDZ domain other than an *inaD*<sup>215</sup> mutation.
- e) activating said signal transduction in said second cell,
- f) detecting said signal transduction from said second cell with a signal transduction detection system, and

g) comparing said signal transduction from said first cell with signal transduction from said second cell, wherein a difference in detected signal transduction from said first cell and said second cell identifies said test chemical as a modulator of signal transduction affected by InaD.

15. (Previously presented): The method of claim 14, wherein said second cell is the same type of cell as said first cell.

Claims 16-42 (Canceled)

43. (Currently Amended): The method of claim 14, wherein the signal transduction protein is a kinase, a phosphatase, a G-protein coupled receptor (GPCR), a tyrosine kinase receptor, a tyrosine phosphatase receptor, an ion channel, a G-protein, a phospholipase or a calcium binding protein.

44. (Previously presented): The method of claim 43, wherein said signal transduction protein is transient receptor potential protein (TRP), protein kinase C, or phospholipase C.

45. (Previously presented): The method of claim 14, wherein the amino acid mutation of said defective InaD is in the first, second, fourth, or fifth PDZ domain.

46. (Previously presented): The method of claim 14, wherein the amino acid mutation of said defective InaD is in the second, fourth, or fifth PDZ domain.

47. (Previously presented): The method of claim 14, wherein the amino acid mutation of said defective InaD is an *inaD*<sup>2</sup> or an *inaD*<sup>1</sup> mutation.

48. (Previously presented): The method of claim 14, wherein the amino acid mutation of said defective InaD is in the third PDZ domain and signal transduction is activated with light and detected by detecting an altered latency period.

49. (Previously presented): The method of claim 14, further comprising:

- h) contacting a third cell with said test chemical, wherein said third cell comprises said signal transduction protein and a polynucleotide encoding a defective InaD, said defective InaD fails to functionally bind at least one signal transduction protein to permit or enhance signal transduction, and wherein said defective InaD of said third cell comprises a mutation in a PDZ domain, and said defective InaD of said second cell comprises a mutation in a different PDZ domain,
  - i) activating said signal transduction in said third cell,
  - j) detecting said signal transduction from said third cell with a signal transduction detection system, and
  - k) comparing signal transduction from said first cell with signal transduction from said second cell and signal transduction from said third cell, wherein a difference in detected signal transduction between said second cell and said third cell is informative of the signal transduction pathway affected by the modulator.

50. (Previously presented): A method of identifying a modulator of signal transduction affected by Inactivation No Afterpotential D (InaD), comprising:

- a) contacting a first cell with a test chemical,  
wherein said first cell comprises at least one signal transduction protein and a polynucleotide encoding a transducisome protein, and said transducisome protein functionally binds to said signal transduction protein to permit or enhance signal transduction, and wherein said transducisome protein is an InaD polypeptide of SEQ ID NO:1,
  - b) activating said signal transduction in said first cell,
  - c) detecting said signal transduction from said first cell with a signal transduction detection system,

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d) contacting a second cell with said test chemical,

wherein said second cell comprises said signal transduction protein and a polynucleotide encoding a defective InaD, said defective InaD fails to functionally bind at least one signal transduction protein to permit or enhance signal transduction or said second cells fails to express said InaD polypeptide to permit said InaD polypeptide to functionally bind to at least one signal transduction protein to permit or enhance signal transduction,

e) activating said signal transduction in said second cell,

f) detecting said signal transduction from said second cell with a signal transduction detection system, and

g) comparing said signal transduction from said first cell with signal transduction from said second cell, wherein a difference in detected signal transduction from said first cell and said second cell identifies said test chemical as a modulator of signal transduction affected by InaD.